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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,587	12/04/2001	Michael A. Tainsky	0788.00063	5172

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EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,587	TAINSKY ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 10-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III. in the reply filed on 26 April 2004 is acknowledged. The traversal is on the ground(s) that all Group s are classified in class 435 and that all methods relate to detecting or selecting specific combinations of markers. This is not found persuasive for the reasons set forth in the Previous Office Action. Namely, the inventions are unrelated because they are not disclosed as capable of use together and they have different modes of operation, different functions, and different effects

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The Information Disclosure Statement filed 8 August 2003 has been partially considered. The following references have not been considered because they are missing from the file: Berek (1991); Buettner (1993); Kohonen (1995); and Poggio (1990). Applicant is kindly requested to send these references with the next response. A signed copy of PTO Form 1449 is included with this Office Action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It was not executed in accordance with either 37 CFR 1.66 or 1.68. There are no signatures for either inventor.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to detect a combination of markers for diagnosing the presence of a disease by selectively biopanning sera obtained from a patient to obtain cDNA clones to array. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification provides a definition for "biopanning" at page 16. Biopanning is defined, as it is in the art, as "a selection process for use in screening a library". "Biopanning is carried out by incubating phages encoding the peptides with a plate coated with

proteins, washing away the unbound phage, eluting, and amplifying the specifically bound phage.

In the instant specification, sera from both normal individuals and patients having ovarian cancer and phage display libraries expressing cDNAs of gene expressed in ovarian epithelial tumors and cell lines are used. This provides for the identification of epitope bearing phage clones displaying reactivity with antibodies present in sera of patients with ovarian cancer but not in control sera (page 25).

The instant claims, however are drawn to biopanning sera to obtain cDNA, without any indication about what proteins are used or peptides or phage. There is no indication in the specification that biopanning sera can be used to isolate cDNA clones. One of skill in the art would not know how to perform the steps of the method to obtain cDNA using the guidance in the specification. The guidance in the specification identifies epitopes which are reactive to antibodies, which could conceivably be the markers intended for detection, but this is not clear. The claims are not directed to such identification and detection of antibodies. Furthermore, the instant claims do not provide for a phage library in which the expressed genes are from known tumors or cell lines. Without known phage libraries, how can one identify specific markers? One would have to know that the expressed genes are linked to a disease state.

One of skill in the art would then turn to the prior art to practice the claimed invention. The prior art teaches that biopanning is carried out by incubating a pool of phage-displayed protein variants with an immobilized target, washing away the unbound phage, and specifically eluting the bound phage. Or the phage can be biopanned against a target in solution, followed by affinity capture of the target-phage complex. The eluted phage is then amplified and taken

through additional cycles of binding and amplification, which will successively enrich the pool of eluted sequences in favor of the tightest binding clones. After 3-4 rounds, individual clones are characterized by DNA sequencing (The NEB Transcript (1996) Vol. 8, No. 1, pages 1-5). The claims of the instant invention, however, are drawn to biopanning sera and obtaining cDNA. There is no indication of a known target in the instant claims, such that binding and elution would yield any meaningful result. Clones are identified in the prior art because targets are known such that they are associated with a desired quality.

Furthermore, how does one determine if markers are present among cDNA clones, when the markers are not known? Where do the markers come from? Are they pre-determined to be associated with a certain disease state? How are the markers identified?

How are markers determined by automatic analysis? How are markers determined by software without any physical assay indication of the presence of a marker?

How are classifiers constructed for this analysis? There is no guidance in the specification as to how classifiers for markers detection are indicated.

d) The invention is drawn to methods of detecting markers for disease diagnosis.

e) The state of the prior art is indicated above.

f) The skill of those in the art of molecular biology is high.

g) The prior art is predictable because precise steps are included to go from biopanning a phage library to isolation of clones which are then characterized by sequencing.

h) The claims are broad because they encompass a method that appears to be missing steps. The skilled practitioner would first turn to the instant specification for guidance to practice methods of biopanning to obtain cDNA. However, the instant specification does not provide

specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that the phage is biopanned against a target. Finally, said practitioner would turn to trial and error experimentation to determine if biopanning sera from a patient without any known target or reference can obtain cDNA clones useful to identify markers for disease. Such represents undue experimentation

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites "selectively biopanning". It is unclear what is meant by "selectively". Does this mean that only certain sera are used? Clarification is requested. It is also unclear what one is biopanning for? (see 112, 1st rejection above)

Claim 7 appears to be missing steps and it is unclear what limitations or steps are intended by the instant claim. (see 112, 1st rejection above) Clarification is requested.

It is unclear, in claim 7, what is meant by "determining if markers are present". What is meant by "determining"? Detecting a marker for intensity or some other definition? Clarification is requested.

Claim 9 recites "earlier screens". It is unclear how this relates to claim 7 because there are no "earlier screens" that take place. There is insufficient antecedent basis for this in the claims.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

MARJORIE MORAN
PATENT EXAMINER

July 8, 2004
Lori A. Clow, Ph.D.
Art Unit 1631